Prenatally Diagnosed Ureteropelvic Junction Obstruction in Three Siblings of one Family: A Case Report

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Ureteropelvic junction obstruction is a rare congenital abnormality. The mode of inheritance is thought to be autosomal dominant with variable expressivity. Here, a consanguineous family whose three siblings diagnosed to have various degree of ureteropelvic junction obstruction is presented. Ureteropelvic junction obstruction may have a genetic background and may recur in subsequent pregnancies. Furthermore, genetic thrombophilias may be associated with urinary abnormalities. Further molecular studies are necessary to prove that finding.

Key Words: Ureteropelvic junction obstruction, Fetal urine aspiration, In vitro fertilization and congenital abnormalities, Familial uretereal abnormalities, Thrombophilia

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Introduction

Ureteropelvic junction obstruction (UPJO) is a rare congenital ureteral abnormality. The mode of inheritance is thought to be autosomal dominant with variable expressivity.[1, 2] This entity may also be included in some familial conditions such as familial ureteral abnormalities syndrome (FUAS) which consists of vesico ureteral reflux, ureteropelvic junction obstruction, duplicated ureters and medullary sponge kidney. Molecular studies in this field are rare. Some linkage analysis related to FUAS and ureteral anomalies demonstrated a genetic heterogeneity in HLA1. But some studies don't show any linkage of HLA haplotypes on chromosome 6 in familial hydronephrosis. Thus, HLA haplotyping is not necessary in predicting prevalence of renal obstruction.

Early recognition of ureteral obstructive pathologies is important both for follow up and planning of invasive procedures, because they may result in irreversible changes on renal functions. Some studies reveal that in fetal hydronephrosis caused by upper urinary tract pathologies, early interventions such as interval fetal urine aspiration or vesico amniotic shunts are useful for saving fetal renal function.[1]

Here, a family with three consecutive siblings which are affected (first sibling diagnosed to have multiple anomalies including bilateral pelviectasis and the last two siblings diagnosed to have bilateral renal pelviectasis) by UPJO will be reported.

Case Report

Thirty eight year old mother was admitted to our hospital for the follow up of her third pregnancy at 12 weeks 6 days of gestational age. The couple was having a third degree consanguinity and because of fertility problems they have applied for assisted reproductive techniques several times. The first three attempts of In Vitro Fertilization were unsuccessful, at the fourth attempt of IVF, conception was achieved.

Her first pregnancy was achieved through IVF at the fourth attempt. During the follow-up prenatal ultrasonography (USG) revealed that the fetus had hemivertebrae (L5-S1), unilateral renal hypoplasia, bilateral UPJO and Atrial Septal Defect. Pregnancy was terminated at 24 weeks 2 days of gestational age. The case was consulted with genetics because fetal autopsy had revealed multiple anomalies including hemivertebrae (L5-S1), anal atresia, atrial septal defect, left atrial isomerism, hypoplastic-cystic dysplastic left kidney, and bilateral UPJO and single umbilical artery. The fetus was thought to be a possible VATER's (Vertebral Defects, Anal Atresia, Tracheo-Esophageal Fistula, and Renal Dysplasia) association. Chromosomal analysis of fetus was 46XX, and the maternal and paternal karyotypings were normal.

Her second pregnancy was result of a spontaneous fertilization after 2 attempts of IVF. During follow up, mother had been detected to have thrombophilia and was treated with Low

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Molecular Weight Heparin (LMWH), low dose aspirin and Vitamin B complex. At 20th week, prenatal ultrasonography revealed bilateral renal pelviectasis suggesting bilateral UPJO. Amniocentesis was performed and resulted a normal karyotype. During follow-up, bilateral renal pelviectasis persisted but their size did not increase. Gestation resulted with delivery of a 3500g male fetus at 36 weeks 3 days. After delivery, at 40th day of life the baby need an intervention due to increased pelviectasis and underwent pyeloplasty operation by pediatric urologists. At 47th day of life, bilateral nephrostomy applied and in the follow up nephrostomy removed .At 3 years old, the child had been noticed to have difficulties in speech, communication and learning. The baby had been diagnosed to have atypical diffuse developmental defects. Now the baby is at 4 years old with normal renal function.

Her last pregnancy was achieved spontaneously. Because of advanced maternal age amniocentesis performed and resulted a normal karyotype. Prenatal ultrasonography at 19th gestational age revealed bilateral mild pelviectasis with an antero-posterior renal pelvic diameter of 5.5mm. In the follow-up, at 24th week of gestation, antero-posterior renal pelvic diameter was 7.5mm on left and 8mm on the right. At 34th gestational age right renal pelvic anteroposterior diameter was 8.5 mm and left renal pelvic anteroposterior diameter was 7.6 mm. No intervention applied during follow-up period. At 38th week of gestation, a 3830 gram male baby was born. In the follow up of the newborn, right renal pelvic dilatation persisted but left renal pelvic dilatation regressed. The baby is still under control of pediatric nephrology unit, without any other developmental problems.

Discussion

Fetal hydronephrosis is known to be the most common cause of abdominal mass and also one of the most commonly detected fetal anomaly at prenatal ultrasound[3]. The diagnosis depends on sonographic findings but even the diagnostic cut off values are still a debate. Several studies on this issue generally meet at one point that we should consider 4 mm or greater before 33 weeks gestation and 7 mm or greater after 33 weeks of gestation as abnormal5. Because UPJO causes greater degree of dilatation among the other causes of hydronephrosis, higher cut off values can cause misdiagnosis of pathologies like Vesico-ureteral reflux or extrarenal pelvis, which may also need postnatal follow up or intervention to prevent renal function deterioration.[3]

Although antenatal USG has a high sensitivity in diagnosis and follow-up of fetal renal pathologies, it has a relatively lower specificity for detecting specific pathology. This may be an important point when you're planning the treatment algorithm. Correct strategy depends on specification of the pathology, the degree of functional deterioration and determination of causes accordingly.

Fetal blood sampling and analysis of some parameters including some electrolytes, urea, and creatinine may be an option but one must remember that plasenta behaves like a natural dialysis unit. β2-Microglobulin, the light chain of class 1 MHC antigens may be used for that purpose. It doesn't cross placenta, is filtered by glomerulus and 99% is reabsorbed by proximal renal tubule4. This is a parameter which can reflect both glomeruler and tubular functions of fetal kidney. Fetal urine sampling is another method may be used in urinary pathologies to achieve proper case selection .Fetal renal kidney produces more hypotonic urine as it maturates. Hypertonic urine regarded as a reflection of nephron malfunction or renal dysplasia.[5]

In this report, we presented a consanguineous family from Turkey in which three siblings were affected consecutively with UPJO, being the second family in the medical literature.[2] There's one study displaying the positive relationship between consanguinity, history of congenital abnormalities among the family members and fetal urinary tract abnormalities; underlining the importance of early detection of urinary tract pathologies in order to provide preventive approach against deterioration of renal functions6. Some form of urinary tract abnormalities may have a genetic background which may be expressed in an autosomal dominant manner and may recur in siblings of consanguineous family. Further molecular studies are necessary to prove that finding.

One of sibling was result of conception after in vitro fertilization. We know that risk of some congenital abnormality increases in the pregnancy achieved by IVF procedure.[7, 8] Furthermore, in this family we noticed that the mother had thrombophilia. There is no information about the increased risk of congenital renal pathologies and thrombophilia in medical literature. It will be a speculation to state that some form of thrombophilia may have an association with congenital anomalies but this issue may need some attention. Further studies are necessary to prove this association.

Bir Ailenin Üç Çocuğunda Prenatal Tanısı Yapılan Ureteropelvik Bileşke Darlığı

Ureteropelvik bileşke darlığı nadir görülen bir doğumsal anomalidir. Kalıtım şeklinin değişken geçişli otozomal dominant yol olduğu düşünülmektedir. Burada üç çocuğu da değişken derecelerde ureteropelvik bileşke darlığı tanısı almış olan, akraba evliliği yapmış bir aile sunulmaktadır. Ureteropelvik bileşke darlığının genetik bir tabanı olabileceği ve takip eden gebeliklerde tekrar görülebileceği düşünülmektedir. Ayrıca kalıtımsal trombofililerin üriner anomaliler ile ilgili olabileceği düşünülmüştür. Bu ilişkileri kanıtlamak için daha fazla moleküler çalışmaya ihtiyaç vardır.

Anahtar kelimeler: Üreteropelvik bileşke darlığı, Fetal idrar örneklemesi, In vitro fertilizasyon ve konjenital anomaliler, Ailesel üreteral anomaliler, Trombofili

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